UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/771,833	02/03/2004	Dean R. Artis	039363-1106	9734

30542 7590 03/02/2007

FOLEY & LARDNER LLP
P.O. BOX 80278
SAN DIEGO, CA 92138-0278

EXAMINER	
KIM, ALEXANDER D	
ART UNIT	PAPER NUMBER
1656	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/02/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/771,833	ARTIS ET AL.	
	Examiner	Art Unit	
	Alexander D. Kim	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 November 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) *10-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/20/2006, 08/17/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Application Status

1. In response to the previous Office actions, a non-Final rejection (mailed on 07/14/2006), Applicants filed a response and amendments received on 11/20/2006. Said amendment amended Claims 1-2, 4, and 7 and withdrawn Claims 10-25. Thus, Claims 1-25 are pending in the instant Office action. Claims 1-9 are examined herein.

Information Disclosure Statement

2. The information disclosure statements (IDS) filed on 11/20/2006 and 08/17/2006 have been reviewed, and its references have been considered as shown by the Examiner's initials next to each citation on the attached copy.

Withdrawn-Compliance with Sequence Rules

3. The Non-compliance of sequence rules for structural coordinates in Table 1 is withdrawn by the virtue of Applicants amendment.

4. The Non-compliance of sequence rules for Tables 2-4 disclose amino acid sequences and/or a nucleic acid sequence is withdrawn by the virtue of Applicants' amendment to the specification received on October 26th, 2004, as cited by the Applicants.

Withdrawn-Objections to the Specification

5. The previous objection of specification because the title is not descriptive of the elected claims is withdrawn by the virtue of Applicants amendment.

6. The previous objection of Abstract for not completely describing the disclosed subject matter is withdrawn by the virtue of Applicants amendment and agreement reached on previous telephone interview on 24 October 2006.

7. The previous objection because PDE5A is used for catalytic domain of PDE5 is withdrawn in view of further consideration of the term "PDE5A" is known prior to the instant application (see Table 4 in the specification) and the definition of the Applicants in page 10, middle.

8. The previous objection of an equation for Ki disclosed in bottom of pp. 92 is withdrawn by the virtue of Applicants amendment.

9. The previous objection of specification for not being in the appropriate format/titled sections required by MPEP §600 is withdrawn by the virtue of Applicants argument.

10. The previous objection of specification for the disclosure interchangeable use of terms "comprising", "consisting essentially of" and "consisting" in the instant application

pp. 97, § 0342 is withdrawn by the virtue of Applicants argument on page 13, bottom to page 14, top.

Withdrawn-Claim Rejections - 35 USC § 112

11. Previous rejection on Claims 1-9 under of 35 U.S.C. 112, second paragraph, for using terms "comprising", "consisting essentially of" and "consisting" interchangeably is withdrawn by the virtue of Applicants argument on page 14, middle.

12. Previous rejection on Claims 1-3 under of 35 U.S.C. 112, second paragraph, for reciting the limitation "co-crystals" and the missing a critical method steps is withdrawn by the virtue of Applicants amendment.

13. Previous rejection on Claims 2 and 7 under of 35 U.S.C. 112, second paragraph, for reciting the relative term "weak binding compound" and "binds weakly", respectively, is withdrawn by the virtue of Applicants amendment.

14. Previous rejection on Claims 4-9 are rejected under of 35 U.S.C. 112, second paragraph, for Claim 4 reciting the limitation "derivative" is withdrawn by the virtue of Applicants amendment.

Maintained-Claim Rejections - 35 USC § 112

15. Previous rejection on Claims 1-3 under 35 U.S.C. § 112, first paragraph, written

description, is maintained. Applicants' arguments have been fully considered but are not deemed persuasive for the following reasons. Applicants argue that Applicants' method of ligand development provide an "example of a method of obtaining the necessary structure of the co-crystal, where such structure provides adequate information" (see page 17, bottom). Applicants argue that Applicants' invention fully describe "the information from any PDE5A co-crystal" (emphasis added, see page 18, lines 3-4) and process involved with said co-crystal "could be applied to any appropriate co-crystal of PDE5A" (emphasis added, see page 18, lines 6-7). Applicants argue that the method for developing improved ligand requiring step of making any PDE5A co-crystal with any ligand, and providing any structure of ligand in the active site of PDE5A is "clearly in Applicants' possession" (see page 18, line 9). As previously noted, to fully describe a genus of method for developing an improved ligand binding using any PDE5A co-crystal, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed genus, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these. In the absence of structural/functional correlations, one of skill in the art would be unable to predict the structure of the members of the genus form the instant disclosure. As noted in previous office action, Applicants disclose only one species of method using the three-dimensional structure of Table 1 that is the structure of human PDE5A co-

crystallized with Sp-cAMP as disclosed in Example 3, page 91. While MPEP § 2163 acknowledges that in certain situations "one species adequately supports a genus," it is also acknowledges that "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus." The co-crystallization condition of Example 3, cannot be used for crystallization of any other PDE5A and form a protein crystal or co-crystal. Thus, the Applicants example cannot predict the method comprising conditions for crystallization or the co-crystallization of any other PDE5A. For the reasons above, the instant rejection is maintained.

16. Previous rejection on Claims 5-6 under 35 U.S.C. § 112, first paragraph, written description, is maintained. Applicants' arguments have been fully considered but are not deemed persuasive for the following reasons. Applicants argue "that lack of correlation between structure and function are irrelevant to the written description requirement" (see page 19 lines 5-6). However, to fully describe a genus of method for developing any improved ligand binding to PDE5A, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed genus, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these. Thus, the correlation between structure and

function are important for adequate written description requirement. In the absence of structural/functional correlations, one of skill in the art would be unable to predict the structure of the members of the genus (i.e., any compound and/or its derivative) form the instant disclosure. Applicants also argue that "Applicants have provided adequate description of the claimed method, providing structure to the compounds" and "ability to modify structure to provide ligands with greater specificity" (see page 19, lines 8-9). For the reasons above, the instant rejection is maintained.

17. Previous rejection of Claims 1-3 under 35 U.S.C. 112, first paragraph, scope of enablement is maintained. Applicants' arguments have been fully considered but are not deemed persuasive for the following reasons. Applicants argue the reference of Ho et al. "makes no mention of ligand development of any kind" (see page 20, top). Applicants acknowledge that "a co-crystal is, therefore, a precondition to carrying out the claimed method" (see Remarks page 20, lines 16-17) and recite that "If no such co-crystal exists, one would not apply the invention method" (see Remarks page 20, lines 17-18). However, the Applicants argue that "the exemplary co-crystal and described methods of making such crystals should not limit the scope of these claims" which contradicts to the not being able to carry out the claimed method without a co-crystal of PDE5A and a compound. Applicants disclose that "Applicants do not claim crystallization of any and all PDE5A with suitable compounds, rather, Applicants claim a method of using such crystals once they are formed" (see Remarks, page 21, lines 1-2). According to MPEP 2106, "The claimed invention as a whole must >be useful and<

accomplish a practical application. That is, it must produce a "useful, concrete and tangible result." State Street, 149 F.3d at *>1373-74<, 47 USPQ2d at 1601-02. The purpose of this requirement is to limit patent protection to inventions that possess a certain level of "real world" value, as opposed to subject matter that represents nothing more than an idea or concept, or is simply a starting point for future investigation or research (Brenner v. Manson, 383 U.S. 519, 528-36, 148 USPQ 689, 693-96 **> (1966); In re Fisher, 421 F.3d 1365, 76 USPQ2d 1225 (Fed. Cir. 2005); In re Ziegler, 992 F.2d 1197, 1200-03, 26 USPQ2d 1600, 1603-06 (Fed. Cir. 1993))". However, as it is written, the claims encompass a process comprising any PDE5A co-crystal for determining a structural information, which is not fully enabled other than the process comprising the Table 1 describing the co-crystal of human PDE5A and Sp-cAMP. In addition, Applicants are seeking to a patent representing a starting point for future investigation or research by the underlined portion of Remarks above (i.e., "once they are formed"). Furthermore, the Applicants position of intended scope of invention is not clear in view of the Applicants disclosure of a method which "could be applied to any appropriate co-crystal of PDE5A" as recited in the argument for Written Description rejection as disclosed above. Applicants argue that "Based on Applicants disclosure, the experimentation necessary to develop such ligands is not undue"; therefore, a large experimentation is not necessarily undue experimentation" because "all of the necessary experimentation is routine to these skilled artisans collectively" (see page 22, top) including "preparing co-crystals" (see bottom of page 22). However, as acknowledged by the Applicants, the claimed method requires a co-crystal of PDE5A,

and crystallization of any PDE5A co-crystal to provide a structural information of PDE5A for a method of finding an improved ligand is unpredictable and requires undue experimentation as disclosed in the previous Office Action. The process of making the Applicants' PDE5A co-crystal in Example 3 would not enable a skilled artisan to make and use the entire scope of the claimed invention requiring any PDE5A co-crystal for developing an improved ligand. For the reasons above, the instant rejection is maintained.

New-Claim Rejections - 35 USC § 112

18. Claims 4-9 are rejected under 35 U.S.C. § 112, first paragraph, written description, necessitated by the amendment, for the same reasons noted in previous office action NO. 11 and herein for the same rejection of Claims 1-3 because the Claims 4-9 reads on a method using any co-crystal of PDE5A and a compound.

19. Claims 4-9 are rejected under 35 U.S.C. § 112, first paragraph, scope of enablement, necessitated by the amendment, for the same reasons noted in previous office action NO. 13 and herein for the same rejection of Claims 1-3 because the Claims 4-9 reads on a method using any co-crystal of PDE5A and a compound.

20. Claims 2 and 7 are rejected under 35 U.S.C. 112, first paragraph, new matter, as failing to comply with the written description requirement. The claim(s) contain subject matter, which was not described in the specification in such a way as to reasonably

convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is necessitated by the amendment.

The instant claims 2 and 7 recites the limitation of 1 uM to about 1 mM. Applicants disclose and argue that this range is supported by the disclosure in page 50 §0184. However, the said page only disclose ranges of "greater than 1 uM" (i.e., greater than 1 uM to unlimited concentration), "above about 100 uM" (i.e., 100 uM to unlimited concentration), and "above about 1 mM" (i.e., 1 mM to unlimited concentration), which are different from the range of "1 uM to about 1 mM". The applicant is advised to point out the support in the original disclosure or amend the instant claims.

Withdrawn-Claim Rejections - 35 USC § 102

21. Previous rejection of Claims 4-9 rejected under 35 U.S.C. 102(a) as being anticipated by Rascon et al. (PNAS (2002) Vol. 99(7), pp. 4714-4719) as evidenced by Turko et al. (Mol Pharmacol (1999) Vol. 56, pp. 124-130) is withdrawn by the virtue of amendment.

Maintained-Claim Rejections - 35 USC § 102

22. Previous rejection of Claims 1, 3-6, 8-9 under 35 U.S.C. 102(b) as being anticipated by Ho et al. (The EMBO Journal (2000) vol. 19(20), pp. 5288-5299) is maintained. Applicants' arguments have been fully considered but are not deemed

persuasive for the following reasons. Applicants argue "Ho et al. makes no mention of ligand development of any kind" and "absolutely no disclosure of Applicants' method steps for providing an improved ligand" (see Remarks on page 24, lines 6 and 8). However, as the claims are written, providing an improved ligand is not a limitation of claims. Ho et al. teach the importance of a ligand binding ",either covalent or non-covalent, of a remarkably diverse set of regulatory small molecules" and "The putative ligands for many of the PAS and GAF domains remain unidentified, suggesting that there still exists a wealth of yet-to-be-discovered small molecule" (see top of left column, p. 5297), which is clear indication of "ligand development of any kind". As noted in the previous office action, Ho et al. teach Applicants' method steps including amended step of "testing the compound for binding to PDE5A" in Claim 1 by teaching "cGMP binding assays" in the Materials and methods in page 5297, bottom of left column. Applicants also argue Ho et al. do not "includes the steps of identifying a chemical structure on the cGMP that can be modified to alter binding to PDE" and "modifying such structure to provide a ligand such as cAMP". Thus, applicants argue "Ho et al. simply discloses compounds that bind to PDE" and "does not suggest that cGMP and cAMP represent a molecular scaffold and modified molecular scaffold as taught by Applicants' specification and claims" (see Remarks on page 24 middle). As noted in previous Office Action page 14, middle, the "Figure 7A and close up view of cGMP binding site of the PDE5 in Fig. 7B (see page 5295 left column)" is the results of the step of identifying a chemical structure of cGMP by Ho et al. which results in alteration of binding to PDE "when modified" (as recited in Claim 1) in view of specific interactions (or binding)

between cGMP and PDE5. The cGMP and cAMP used in method of Ho et al. are structurally distinct, thus meets the limitation of a molecular scaffold and a modified molecular scaffold. For the reasons above, the instant rejection is maintained.

Summary of Pending Issues

23. The following is a summary of the issues pending in the instant application:

a. Claims 1-3 stand rejected under 35 U.S.C. § 112, first paragraph, written description.

b. Claims 5-6 stand rejected under 35 U.S.C. § 112, first paragraph, written description.

c. Claims 1-3 stand rejected under 35 U.S.C. 112, first paragraph, scope of enablement.

d. Claims 4-9 are newly rejected under 35 U.S.C. § 112, first paragraph, written description.

e. Claims 4-9 are newly rejected under 35 U.S.C. § 112, first paragraph, scope of enablement.

f. Claims 2 and 7 are newly rejected under 35 U.S.C. 112, first paragraph, new matter, as failing to comply with the written description requirement.

g. Claims 1, 3-6, 8-9 stand rejected under 35 U.S.C. 102(b) as being anticipated by Ho et al.

Conclusion

24. Claims 1-9 are not allowed for the reasons identified in the numbered sections of this Office action. Applicants must respond to the objections/rejections in each of the numbered section in this Office action to be fully responsive in prosecution.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alexander D. Kim whose telephone number is (571) 272-5266. The examiner can normally be reached on 8AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr Bragdon can be reached on (571) 272-0931. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Alexander Kim
February 16, 2007

KATHLEEN M. KERR, PH.D.
SUPERVISORY PATENT EXAMINER